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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/673,070	09/26/2003	James Eberwine	RPEN-0005	9287

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EXAMINER	
GIBBS, TERRA C	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 10/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/673,070	EBERWINE ET AL.	
	Examiner	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *September 26, 2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim 1 is pending in the instant application.

Claim 1 has been examined on the merits.

Information Disclosure Statement

Applicant's information disclosure statement filed September 26, 2003 is acknowledged. The references referred to therein have been considered on the merits.

Priority

It is noted that the instant application is a continuation of USSN 09/464,270, filed December 17, 1999, now abandoned.

Specification

The specification is objected to because of the following informalities: The priority information listed in the first sentence of the specification is not updated. This information should refer to the current status of each Application. For example, USSN: 09/464,270 should be referred to as "now abandoned". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claim 1 is drawn to a composition for decreasing glutamate receptor numbers in dendrites of neurons comprising an antisense oligonucleotide or a ribozyme linked to an antisense oligonucleotide, wherein said antisense oligonucleotide is specifically targeted to a dendrite-localized mRNA that encodes for said glutamate receptor which decreases mRNA translation of said glutamate receptor in dendrites of neurons.

The invention encompasses antisense oligonucleotide compositions that encode all forms of glutamate receptors, which includes sequences form other species, mutated sequences, polymorphic and allelic variants, splice variants, sequences that have an unspecified degree of identity (similarity, homology) and so forth. The art teaches glutamate receptors with many different GenBank Accession Numbers. For example, the art teaches Mus musculus glutamate receptor, metabotropic 1 (Grm1), mRNA (GenBank Accession No. NM_016976); Mus musculus glutamate receptor, ionotropic, N-methyl D-aspartate-like 1A (Grinl1a), mRNA (GenBank Accession No. NM_178602);

Mus musculus glutamate receptor, ionotropic, kainate 1 (Grik1), mRNA (GenBank Accession No. NM_146072); Rattus norvegicus glutamate receptor subunit GluR1 gene (GenBank Accession No. AF302117); Homo sapiens glutamate receptor subunit 3 (GRIA3) gene (GenBank Accession No. AF159262); Rattus norvegicus glutamate receptor, ionotropic, kainate 1 (Grik1), mRNA (GenBank Accession No. NM_017241); Mus musculus glutamate receptor, ionotropic, NMDA2C (epsilon 3) (Grin2c), mRNA (GenBank Accession No. NM_010350); Homo sapiens glutamate receptor, ionotropic, AMPA 2 (GRIA2), mRNA (GenBank Accession No. NM_000826); Homo sapiens glutamate receptor, metabotropic 2 (GRM2), mRNA (GenBank Accession No. NM_000839); Homo sapiens glutamate receptor, ionotropic, delta 1 (GRID1), mRNA (GenBank Accession No. NM_017551); Mus musculus glutamate receptor, ionotropic, AMPA4 (alpha 4) (Gria4), mRNA (GenBank Accession No. NM_019691); Mus musculus glutamate receptor, ionotropic, AMPA1 (alpha 1) (Gria1), mRNA (GenBank Accession No. NM_008165); Homo sapiens glutamate receptor, ionotrophic, AMPA3 (GRIA3), transcript variant flip, mRNA (GenBank Accession No. NM_007325); Homo sapiens glutamate receptor, ionotropic, AMPA1 (GRIA1), mRNA (GenBank Accession No. NM_000827); Homo sapiens glutamate receptor, metabotropic 1 (GRM1), mRNA (GenBank Accession No. NM_000838); Homo sapiens glutamate receptor, ionotropic, N-methyl D-aspartate 2A (GRIN2A), mRNA (GenBank Accession No. NM_000833); Homo sapiens glutamate receptor, ionotropic, kainate 5 (GRIK5), mRNA (GenBank Accession No. NM_002088); Homo sapiens glutamate receptor, ionotropic, kainate 5 (GRIK4), mRNA (GenBank Accession No. NM_014619); Homo sapiens glutamate

receptor, ionotropic, kainate 5 (GRIK3), mRNA (GenBank Accession No. NM_000831); Homo sapiens glutamate receptor, ionotropic, N-methyl D-aspartate 1 (GRIN1), transcript variant NR1-3, mRNA (GenBank Accession No. NM_0073); and Homo sapiens glutamate receptor, metabotropic 6 (GRM6), mRNA (GenBank Accession No. NM_000843), for example. There is no disclosure found in the specification or known in the art that relates the structure of a composition for decreasing glutamate receptor numbers in dendrites of neurons comprising an antisense oligonucleotide or a ribozyme linked to an antisense oligonucleotide, wherein said antisense oligonucleotide is specifically targeted to a dendrite-localized mRNA. The claims are directed to encompass a broad range of antisense oligonucleotides or ribozymes linked to an antisense oligonucleotide of highly variant structures (e.g. nucleic acid sequence), which have not been described in the specification and whose structure could not be envisioned by the skilled artisan based on the disclosure of the specification.

The specification fails to describe the complete structure of a representative number of species of the claimed genus. See the Guidelines for Examination of Patent Applications Under the 35 USC 112 ¶ 1, "Written Description" Requirement (Vol. 66, No. 4, pages 1099-1111). These guidelines state that: "To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set

forth the claimed invention. Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that applicant was in possession of the claimed invention." In the instant case, the specification does not describe or identify characteristics that can be used to distinguish species of the claimed genus.

Additionally, "[T]he skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence."

Applicant's specification does not provide a sufficient number of representative species of compositions for decreasing glutamate receptor numbers in dendrites of neurons comprising an antisense oligonucleotide or a ribozyme linked to an antisense oligonucleotide, wherein said antisense oligonucleotide is specifically targeted to a dendrite-localized mRNA, which would allow one of skill in the art to predict the structures of all members of the claimed genus of oligonucleotide compositions. One of

skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Therefore, the specification does not describe the claimed oligonucleotide compositions in such full and concise terms so as to indicate that the applicant had possession of these compositions at the time of filing of this application. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Hirano et al. (Neuroscience Letters, 1994 Vol. 182:172-176).

Claim 1 is drawn to a composition for decreasing glutamate receptor numbers in dendrites of neurons comprising an antisense oligonucleotide or a ribozyme linked to an antisense oligonucleotide, wherein said antisense oligonucleotide is specifically targeted to a dendrite-localized mRNA that encodes for said glutamate receptor which decreases mRNA translation of said glutamate receptor in dendrites of neurons.

Hirano et al. disclose the involvement of the glutamate receptor subunit in the long-term depression of glutamate responsiveness in cultured rat Purkinje neuronal cells (see Abstract). Hirano et al. further disclose an antisense oligonucleotide against the glutamate receptor δ2 subunit mRNA, which is selectively expressed only in Purkinje neurons, suppressed the induction of long-term depression (LTD) of glutamate responsiveness in the rat cerebellar culture (see Figure 2). Hirano et al. also teach at page 174, second column:

> "Very strong punctuate stainings were observed in dendrites, where granule neurons form synapses both *in vivo* and in culture, and weak in cell bodies, where granule cells do not form synapses. This subcellular localization of the δ2 subunit is consistent with an idea that the δ2 plays a role in the LTD. All these punctuate labelings were abolished by preabsorption of the antibody with the fusion protein. After the treatment with the antisense oligonucleotide, the staining became fainter (Figure 3), although the reduction of staining intensity was not always as obvious".

Therefore, Hirano et al. anticipates claim 1 of the instant invention.

Claim 1 is rejected under 35 U.S.C. 102 (b) as being anticipated by Vanderklish et al. (Synapse, 1992 Vol. 12:333-337).

Vanderklish et al. disclose the translational suppression of a glutamate receptor impairs long-term potentiation (see Abstract). Vanderklish et al. further disclose that glutamate receptor 1 (GluR1) antisense inhibited protein expression (see Figures 1A and 1B) and decreased heterosynaptic potentiation in hippocampal neuronal cultured slices (see Figures 2 and 3).

Therefore, Vanderklish et al. anticipates claim 1 of the instant invention.

Claim 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Oguro et al. (Journal of Neuroscience, 1999 Vol. 21:9218-9227).

Oguro et al. disclose the antisense knockdown of glutamate receptor 2 (GluR2) expression causes delayed neurodegeneration and increases damage by sublethal ischemia in hippocampal neurons (see Abstract). Oguro et al. also disclose that down regulation of GluR2 by antisense decreases GluR2 mRNA and protein levels (see Figures 3 and 4, respectively). Oguro et al. further disclose that a reduction in the level of GluR2 is sufficient to induce delayed death of specific neuronal populations.

Therefore, Oguro et al. anticipates claim 1 of the instant invention.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached on 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

tcg
October 12, 2005

SEAN McGARRY
PRIMARY EXAMINER
1635